

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

THIS PAGE BLANK (USPTO)

(19)



Europäisches Patentamt

European Patent Office

Office européen des brevets



(11)

EP 1 084 619 A1

(12)

EUROPEAN PATENT APPLICATION

(43) Date of publication:
21.03.2001 Bulletin 2001/12

(21) Application number: **00307660.1**

(22) Date of filing: **05.09.2000**

(51) Int. Cl.⁷: **A01N 43/80**, A01N 25/22,
A01N 59/20
// (A01N59/20, 43:80, 43:50),
(A01N43/80, 43:50)

(84) Designated Contracting States:
**AT BE CH CY DE DK ES FI FR GB GR IE IT LI LU
MC NL PT SE**
Designated Extension States:
AL LT LV MK RO SI

(30) Priority: **14.09.1999 US 153778 P**

(71) Applicant: **ROHM AND HAAS COMPANY**
Philadelphia, Pennsylvania 19106-2399 (US)

(72) Inventors:
• **Ei A'mma, Beverly Jean**
Perkiomenville, Pennsylvania 18074 (US)
• **Nagahashi, Susan Lynn**
Warminster, Pennsylvania 18974 (US)

(74) Representative:
Buckley, Guy Julian
ROHM AND HAAS (UK) LTD.
European Operations Patent Department
Lennig House
2 Mason's Avenue
Croydon CR9 3NB (GB)

(54) **Stable biocidal compositions**

(57) Disclosed are biocidal compositions comprising mixtures of formaldehyde-releasing imidazolidines, such as 1,3-dimethylol-5,5-dimethylhydantoin, and 3-isothiazolones stabilized with low levels of copper salts.

EP 1 084 619 A1

Description

BACKGROUND OF THE INVENTION

[0001] The present invention relates to stable biocidal compositions containing combinations of certain imidazolidines and 3-isothiazolones. The present invention also relates to the use of low concentrations of copper salts to stabilize such compositions.

[0002] Microbicides are used commercially to prevent the growth of microbes in a variety of loci, such as cooling towers, metal working fluid systems, paints and cosmetics. One of the more important classes of microbicides is 3-isothiazolones. Many 3-isothiazolones have achieved commercial success because they are very effective in preventing microbial growth under a wide variety of conditions and in a variety of loci. Among the most important 3-isothiazolones are 5-chloro-2-methyl-3-isothiazolone ("CMI"), 2-methyl-3-isothiazolone ("MI"), and mixtures thereof.

[0003] Although 3-isothiazolones are highly effective microbicides, some suffer from being unstable under certain conditions. Without the presence of a stabilizer, many 3-isothiazolones chemically degrade and lose microbicidal efficacy. Much research has been devoted to stabilizing 3-isothiazolones. A variety of stabilizers for 3-isothiazolone solutions are known and are described, for example, in US 5,461,150 (Girona et al) and US 5,312,827 (Bayer et al).

[0004] Imidazolidines (which include hydantoin) are another class of microbicides, and have been used for years in a variety of loci. The most well-known microbicide of this class is 1,3-dimethylol-5,5-dimethylhydantoin ("DMDMH"). DMDMH is generally provided as an aqueous solution, an anhydrous powder, or a solution in glycol. DMDMH is sold under various names, including Glydant®. These types of compounds are storage stable as supplied and do not require stabilizers to prevent chemical degradation.

STATEMENT OF THE INVENTION

[0005] The present invention is directed to stable biocidal compositions comprising at least one formaldehyde-releasing imidazolidine, at least one 3-isothiazolone, a stabilizing amount of copper ion and solvent.

[0006] The present invention is also directed to a method of stabilizing a biocidal composition containing at least one formaldehyde-releasing imidazolidine and at least one 3-isothiazolone by the addition of a low level of copper ion.

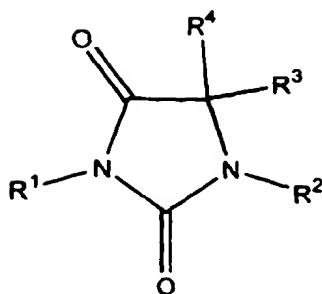
DETAILED DESCRIPTION OF THE INVENTION

[0007] As used in this specification, the term "antimicrobial agent" refers both to a compound capable of inhibiting microbial growth (a preservative), and a compound capable of reducing microbial concentration (a disinfecting agent), within a given system. The term "antimicrobial activity" refers to the activity of the antimicrobial agents to eliminate, inhibit or prevent the growth of microorganisms. The terms "microbial organism," "microbe" and "microorganism" are used interchangeably and refer to microorganisms such as, but not limited to: fungi, bacteria, and algae. The term "locus" or "loci" refers to an industrial system or product subject to contamination by microorganisms. The following abbreviations are used throughout this specification: AI = active ingredient, mL = milliliter; g = grams. Unless specifically identified otherwise in this specification, percentages are by weight, ranges are to be read as inclusive, and ratios are weight ratios.

[0008] The present invention is based in part on the unexpected discovery that addition of 3-isothiazolones to imidazolidine compositions results in destabilization of the imidazolidines. A further unexpected discovery is that such combinations can be stabilized using low levels of copper ion.

[0009] Any 3-isothiazolone compound is useful in the compositions of the present invention. Suitable 3-isothiazolone compounds include, but are not limited to: 5-chloro-2-methyl-3-isothiazolone; 2-methyl-3-isothiazolone; 2-ethyl-3-isothiazolone; 5-chloro-2-ethyl-3-isothiazolone; 4,5-dichloro-2-methyl-3-isothiazolone; 2-n-octyl-3-isothiazolone; 4,5-dichloro-2-n-octyl-3-isothiazolone; 1,2-benzisothiazolone; 4,5-trimethylene-2-methyl-3-isothiazolone; and mixtures thereof. When mixtures of 5-chloro-2-methyl-3-isothiazolone and 2-methyl-3-isothiazolone are used, the weight ratio of 5-chloro-2-methyl-3-isothiazolone to 2-methyl-3-isothiazolone is generally 99:1 to 1:99, preferably 90:10 to 70:30.

[0010] The imidazolidines useful in the compositions of the present invention are any formaldehyde-releasing imidazolidines, particularly those of formula I and oligomers thereof:



wherein:

R^1 and R^2 are independently selected from: H; CH_2OH ; $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkenyl or $\text{C}_1\text{-C}_4$ alkynyl optionally substituted with O, S or N; provided that at least one of R^1 or R^2 is CH_2OH ; and

R^3 and R^4 are independently selected from: H; OH; halogen; $\text{C}_1\text{-C}_3$ alkoxy; $\text{NR}^5\text{C}(\text{O})\text{NHR}^6$; $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkenyl or $\text{C}_1\text{-C}_4$ alkynyl optionally substituted with O, S or N; and

R^5 and R^6 are independently selected from: H; CH_2OH ; $\text{C}_1\text{-C}_4$ alkyl, $\text{C}_1\text{-C}_4$ alkenyl or $\text{C}_1\text{-C}_4$ alkynyl optionally substituted with O, S or N.

[0011] Preferred imidazolidines include diazolidinylurea, imidazolidinyl ureas and the mono- and di-methylol 5,5-dimethylhydantoin. Most preferred is 1,3-dimethylol-5,5-dimethylhydantoin.

[0012] In general, a greater amount of imidazolidine than 3-isothiazolone will be present in the compositions of the present invention. Ratios of imidazolidine to 3-isothiazolone will vary greatly depending on the particular application, but will typically be between 1:1 and 800:1. It is preferred that the imidazolidine to 3-isothiazolone ratio be between 10:1 and 400:1, and most preferably between 75:1 and 333:1.

[0013] A wide variety of copper salts are known in the art. Any copper salt which is sufficiently water soluble to provide the desired level of cupric ion in solution may be used. Suitable examples include, but are not limited to: copper sulfate, copper acetate, copper chloride, copper bromide, copper chlorate, copper perchlorate, copper nitrite and copper nitrate. Copper sulfate and copper nitrate are preferred. The copper salts are generally commercially available, for example, from Pfalz and Bauer (Waterbury, Connecticut) and may be used without further purification.

[0014] The amount of cupric ion useful in the compositions of the present invention is typically 10 to 2500 ppm. The amount of cupric ion is preferably 10 to 1000 ppm, most preferably 10 to 100 ppm. Less cupric ion is needed where there is a lower concentration of 3-isothiazolone. As the concentration of the 3-isothiazolone is increased, proportionally more cupric ion is required to achieve the same stability. In general, the ratio of copper ion to 3-isothiazolone will be between 1:150 and 2:1. It is preferred to have a copper to 3-isothiazolone ratio between 1:75 and 1:1, and most preferably, between 1:15 and 1:5.

[0015] The solvents used in the compositions of the present invention can be water, organic solvent, or mixtures thereof. Any organic solvent is suitable as long as it is compatible with the end use and does not destabilize the antimicrobial agent. Suitable organic solvents include, but are not limited to: aliphatic and aromatic hydrocarbons, such as xylene and mixtures of alkylbenzenes; halogenated aliphatic and aromatic hydrocarbons, such as ethylene dichloride and monochlorobenzene; alcohols, such as monohydric, dihydric, and polyhydric alcohols; aldehydes; ketones, such as acetone, methyl ethyl ketone, and methyl iso-butyl ketone; ethers; glycol ethers; glycol ether acetates; saturated and unsaturated fatty acids having at least four carbon atoms; esters, such as ethyl acetate, butyl acetate, glycol esters, and phthalate esters; and phenols. Preferred organic solvents are glycol ethers; glycol ether acetates; aliphatic and aromatic hydrocarbons; and alcohols. It is more preferred to utilize a mixture of glycol ethers or glycol ether acetates with water. Most preferred is water.

[0016] The compositions of the present invention may also include other stabilizers, such as metal nitrates, iodic acid or its salts, and various other inorganic salts and their like, which will not materially affect the performance of the combination compositions of the present invention. Other types of ingredients which can be included in the biocidal combinations of the present invention may include, without limitation: ethylenediamine tetraacetic acid, benzyl alcohol, phenoxyethanol, methyl or propyl paraben, or other biocides.

[0017] The compositions of the present invention can be used to inhibit the growth of microorganisms by introducing a microbicidally effective amount of the composition onto, into, or at a locus subject to microbial attack. Suitable loci

include, but are not limited to: cooling towers; air washers; boilers; mineral slurries; wastewater treatment; ornamental fountains; reverse osmosis filtration; ultrafiltration; ballast water; evaporative condensers; heat exchangers; pulp and paper processing fluids; plastics; emulsions and dispersions; paints; latexes; coatings, such as varnishes; construction products, such as mastics, caulks, and sealants; construction adhesives, such as ceramic adhesives, carpet backing adhesives, and laminating adhesives; industrial or consumer adhesives; photographic chemicals; printing fluids; household products, such as bathroom disinfectants or sanitizers; cosmetics and toiletries; shampoos; soaps; detergents; surfactants; industrial disinfectants or sanitizers, such as cold sterilants, hard surface disinfectants; floor polishes; laundry rinse water; fabric softeners; metalworking fluids; conveyor lubricants; hydraulic fluids; leather and leather products; textiles; textile products; wood and wood products, such as plywood, chipboard, flakeboard, laminated beams, oriented strandboard, hardboard, and particleboard; petroleum processing fluids; fuel; oilfield fluids, such as injection water, fracture fluids, and drilling muds; agriculture adjuvant preservation; surfactant preservation; medical devices; diagnostic reagent preservation; food preservation, such as plastic or paper food wrap; and pools and spas. Preferred loci are cosmetics and toiletries; latexes; emulsions and dispersions; paints; surfactants; floor polishes; fabric softeners; detergents; and household products.

[0018] The total amount of biocidal actives suitable to inhibit or control the growth of microorganisms will depend on the relative concentrations of imidazolidine and 3-isothiazolone, as well as the locus to be protected, but will generally be between 200 and 7000 ppm, based on the volume of said locus to be protected. It is preferred to use between 500 and 2500 ppm. It is of course within the scope of the present invention that the compositions may additionally include other biocidal actives.

[0019] The following examples are presented to illustrate further various aspects of the present invention, but are not intended to limit the scope of the invention in any respect.

Example 1

[0020] The following is a study of storage stability of combinations of imidazolidine and 3-isothiazolone as compared to either active alone.

[0021] Samples for the combinations were prepared as follows. DMDMH (55 % AI in water) was diluted in distilled water to the appropriate concentration and thoroughly mixed. Stabilizer was added next (the amount based on the amount of Cu^{2+} in $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$), and the sample mixed well. An appropriate amount of 3-isothiazolone (3:1 ratio of CMI:MI) was then melted in a small amount of hot tap water, added to the sample, and then mixed thoroughly. Other samples, i.e., not containing DMDMH, ITA or stabilizer, were prepared in analogous fashion.

[0022] After preparation, each sample was sub-sampled into approximately 10 g glass vials. The vials were then capped, the tops taped, and the vials stored at constant temperature ovens for the duration of the study. Samples were viewed weekly for any visual changes, and aliquots taken at various times during the study. AI levels were measured using HPLC, and remaining percent AI levels determined using the initial measurement (Week 0) as 100% AI.

ID	Ingredients of Composition			AI Remaining			
	% CMI*	% DMDMH	Cu^{2+} (ppm)	4 Weeks @ 55 °C		8 Weeks @ 55 °C	
				% CMI	% DMDMH	% CMI	% DMDMH
A	0.13	---	---	85	---	54	---
B	0.14	---	100	93	---	86	---
C	---	49.3	---	---	93	---	94
D	---	49.4	100	---	92	---	92
E	0.14	49.3	---	50	87	31	82
F	0.15	49.4	100	100	91	100	91

*The ITA used included both MI and CMI, but only the CMI level was measured.

[0023] The results clearly show that the imidazolidine alone is storage stable and does not require the addition of a stabilizer, but that when a 3-isothiazolone is added to the composition, the stability of the imidazolidine is reduced.

Exempl 2

[0024] The following example further demonstrates the storage stability of compositions of the present invention. Samples were prepared in accordance with the procedures of Examples 1, above.

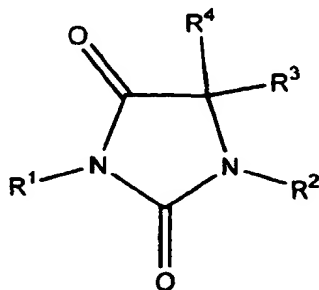
ID	Ingredients of Composition			AI Remaining			
				4 Weeks @ 55 °C		12 Weeks @ 40 °C	
	% CMI*	% DMDMH	CU ²⁺ (ppm)	% CMI	% DMDMH	% CMI	% DMDMH
G	0.18	51.0	---	50	77	44	90
H	0.18	49.2	100	100	100	72	95
J	0.43	37.2	---	9	77	21	85
K	0.48	37.2	100	98	84	75	100

*The ITA used included both MI and CMI, but only the CMI level was measured.

[0025] The results indicate that stability of both DMDMH and the 3-isothiazolones are greatly increased when copper ion is added.

Claims

1. A stable biocidal composition comprising: at least one formaldehyde-releasing imidazolidine; at least one 3-isothiazolone; a stabilizing amount of copper ion; and solvent.
2. The composition of claim 1, wherein the formaldehyde-releasing imidazolidine is of formula I or is an oligomer thereof:



wherein:

- R¹ and R² are independently selected from: H; CH₂OH; C₁-C₄ alkyl, C₁-C₄ alkenyl or C₁-C₄ alkynyl optionally substituted with O, S or N; provided that at least one of R¹ or R² is CH₂OH; and R³ and R⁴ are independently selected from: H; OH; halogen; C₁-C₃ alkoxy; NR⁵C(O)NHR⁶; C₁-C₄ alkyl, C₁-C₄ alkenyl or C₁-C₄ alkynyl optionally substituted with O, S or N; and R⁵ and R⁶ are independently selected from: H; CH₂OH; C₁-C₄ alkyl, C₁-C₄ alkenyl or C₁-C₄ alkynyl optionally substituted with O, S or N.
3. The composition of claim 2, wherein the imidazolidine is selected from the group consisting of: diazolidinylurea, imidazolidinyl ureas, mono-methylol 5,5-dimethylhydantoin, and di-methylol 5,5-dimethylhydantoin.
 4. The composition of claim 1, wherein the 3-isothiazolone is selected from the group consisting of: 5-chloro-2-methyl-3-isothiazolone; 2-methyl-3-isothiazolone; 2-ethyl-3-isothiazolone; 5-chloro-2-ethyl-3-isothiazolone; 4,5-dichloro-2-

EP 1 084 619 A1

methyl-3-isothiazolone; 2-n-octyl-3-isothiazolone; 4,5-dichloro-2-n-octyl-3-isothiazolone; 1,2-benzisothiazolone; 4,5-trimethylene-2-methyl-3-isothiazolone; and mixtures thereof.

- 5 5. The composition of claim 4, wherein the 3-isothiazolone comprises a mixture of 5-chloro-2-methyl-3-isothiazolone and 2-methyl-3-isothiazolone.
6. The composition of claim 1, wherein the weight ratio of copper ion to 3-isothiazolone is between 1:150 and 2:1.
7. The composition of claim 1, wherein the weight ratio of imidazolidine to 3-isothiazolone is between 1:1 and 500:1.
- 10 8. A method of stabilizing a biocidal composition containing at least one formaldehyde-releasing imidazolidine and at least one 3-isothiazolone by the addition of a low level of copper ion.
9. The method of claim 8, wherein the weight ratio of copper ion to 3-isothiazolone is between 1:150 and 2:1.
- 15 10. The method of claim 8, wherein the weight ratio of imidazolidine to 3-isothiazolone is between 1:1 and 500:1.



European Patent
Office

EUROPEAN SEARCH REPORT

Application Number
EP 00 30 7660

DOCUMENTS CONSIDERED TO BE RELEVANT			
Category	Citation of document with indication, where appropriate, of relevant passages	Relevant to claim	CLASSIFICATION OF THE APPLICATION (Int.Cl.7)
Y	US 5 041 457 A (HSU JEMIN C) 20 August 1991 (1991-08-20) * claim 1 *	1-10	A01N43/80 A01N25/22 A01N59/20 //(A01N59/20, 43:80,43:50), (A01N43/80, 43:50)
Y	US 5 464 850 A (VOO LIANN ET AL) 7 November 1995 (1995-11-07) * claim 1 *	1-10	
Y	EP 0 435 439 A (ROHM & HAAS) 3 July 1991 (1991-07-03) * page 1, paragraphs 5,8 *	1-10	
X	WO 98 36049 A (LONZA AG ;COUNTS MICHAEL WAYNE (US)) 20 August 1998 (1998-08-20) * the whole document *	1-10	
The present search report has been drawn up for all claims			TECHNICAL FIELDS SEARCHED (Int.Cl.7)
			A01N
Place of search MUNICH		Date of completion of the search 23 October 2000	Examiner Bertrand, F
CATEGORY OF CITED DOCUMENTS X : particularly relevant if taken alone Y : particularly relevant if combined with another document of the same category A : technological background O : non-written disclosure P : intermediate document		T : theory or principle underlying the invention E : earlier patent document, but published on, or after the filing date D : document cited in the application L : document cited for other reasons & : member of the same patent family, corresponding document	

EPO FORM 1500 03/02 (P4/C01)

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 30 7660

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report. The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

23-10-2000

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
US 5041457	A	20-08-1991	US 4964892 A	23-10-1990
			AT 134477 T	15-03-1996
			AT 173880 T	15-12-1998
			BR 8906719 A	11-09-1990
			CA 2010791 A	10-09-1990
			DE 68925801 D	04-04-1996
			DE 68925801 T	06-02-1997
			DE 68928874 D	14-01-1999
			DE 68928874 T	29-07-1999
			EP 0375367 A	27-06-1990
			EP 0685158 A	06-12-1995
			EP 0685160 A	06-12-1995
			EP 0685159 A	06-12-1995
			ES 2083977 T	01-05-1996
			ES 2124479 T	01-02-1999
			FI 94207 B	28-04-1995
			HU 58469 A	30-03-1992
			IL 92728 A	25-01-1994
			JP 2221205 A	04-09-1990
			JP 2886226 B	26-04-1999
			KR 151952 B	01-10-1998
			PT 92653 B	12-09-1995
			US 5131939 A	21-07-1992
US 5464850	A	07-11-1995	NONE	
EP 0435439	A	03-07-1991	US 5424324 A	13-06-1995
			AT 101962 T	15-03-1994
			AU 643718 B	25-11-1993
			AU 6655990 A	23-05-1991
			BR 9005796 A	24-09-1991
			CA 2029302 A	18-05-1991
			DE 69007052 D	07-04-1994
			DE 69007052 T	21-07-1994
			DK 435439 T	28-03-1994
			ES 2062411 T	16-12-1994
			HU 208945 B	28-02-1994
			IL 96354 A	19-01-1996
			JP 3054874 B	19-06-2000
			JP 3206085 A	09-09-1991
			KR 158368 B	16-11-1998
			NZ 236073 A	27-01-1993
			PL 167760 B	31-10-1995
			SG 58894 G	14-10-1994
			ZA 9009168 A	31-07-1991

EPO FORM P0489

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

**ANNEX TO THE EUROPEAN SEARCH REPORT
ON EUROPEAN PATENT APPLICATION NO.**

EP 00 30 7660

This annex lists the patent family members relating to the patent documents cited in the above-mentioned European search report.
The members are as contained in the European Patent Office EDP file on
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

23-10-2000

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9836049 A	20-08-1998	US 5972864 A	26-10-1999
		AU 6166898 A	08-09-1998
		EP 0966517 A	29-12-1999

EPO FORM P0489

For more details about this annex : see Official Journal of the European Patent Office, No. 12/82

THIS PAGE BLANK (USPTO)